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STEVEN F. WEINSTOCK
ABBOTT LABORATORIES
100 ABBOTT PARK ROAD
DEPT. 377/AP6A
ABBOTT PARK, IL 60064-6008

EXAMINER	
SULLIVAN, DANIEL M	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 12/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/054,534	MUKERJI ET AL.	
	Examiner	Art Unit	
	Daniel M Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *1,6-10 and 17-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-5,11 and 13* is/are rejected.

7)☒ Claim(s) *12 and 14-16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This is the First Office Action on the Merits of the application filed 22 January 2002, which claims benefit as a continuation-in-part of US Patent application 09/769,863 filed 25 January 2001. Claims 1-35 are pending in the application.

Election/Restrictions

Applicant's election of Group I (i.e., Claims 1-7 and 11-16) and SEQ ID NO: 13 in the Paper filed 6 October 2003 is acknowledged. Because applicant did not distinctly and specifically point out errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 8-10 and 17-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention. Further, claims 1, 6 and 7 are also withdrawn from consideration because the claims do not embrace the elected nucleic acid. Claims 2-5 and 11-16 are presently under consideration.

Information Disclosure Statement

The information disclosure statements filed 7 January 2003 and 12 May 2003 fail to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because each listed U.S. Patent must be identified by inventor, patent number and issue date; each listed foreign patent or published application must include the publication date; and each non-patent publication must include a title (see 37 CFR §1.98(b)). It has been placed in the application file, but the

information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

Specification

The disclosure is objected to because of the following informalities: The specification contains numerous trademarks (e.g., paragraph bridging pages 73-74). Trademarks should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

The specification is also objected to because it contains references to dates and deposit numbers that are not specified (e.g., page 69, lines 14 and 16).

The specification is also objected to because it contains typographical errors. In particular, it appears that there is a formatting problem affecting Greek letters (e.g., page 73, line 20).

Claim Objections

Claims 2-5 and 11-16 are objected to because of the following informalities: The claims embrace nonelected subject matter. Specifically, each of the claims is directed to products comprising or methods of using nonelected nucleic acids. Furthermore, claims 15 and 16 encompass the non-elected transgenic plant of Group III. The claims should be amended to remove nonelected subject matter. In particular, claims 15 and 16 should be amended such that they are directed to an isolated plant cell. Appropriate correction is required.

Claims 14 and 16 are additionally objected to because they set forth abbreviations without definition. A definition should be provided for each abbreviation the first time it appears in the claims.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2-5 and 11-16 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5, 10, 16, 17 and 20 of copending Application No. 10/431,952 (hereinafter, '952). Although the conflicting claims are not identical, they are not patentably distinct. Specifically, the limitations of the instant claims 2-

5 are explicitly set forth as embodiments of claims 1-5 in the conflicting application. Likewise, the limitations of the instant claims 11, 12 and 13 are set forth in claims 10, 16 and 17 of the '952 application, respectively. Therefore, the limitations of the instant claims would be obvious to one of ordinary skill in the art from the limitations of the conflicting claims alone.

Furthermore, the instant claims 14-16 are not patentably distinct from claim 20 in the '952 application in light of the teachings of the '952 specification. The instant claims 14-16 are directed to mammalian or plant cells comprising a vector comprising SEQ ID NO: 13, wherein expression of the nucleic acid results in the production of a polyunsaturated fatty acid. Claim 20 of the '952 application is directed to a mammalian or plant cell comprising a vector comprising SEQ ID NO: 13 linked to a promoter. Teachings throughout the '952 specification make clear that the purpose of making a host cell expressing the various desaturase enzymes disclosed therein, including the desaturase encoded by SEQ ID NO: 13, is to produce polyunsaturated fatty acids (see, e.g., page 14, lines 12-22). Thus, the additional limitation of claim 20 to expression resulting in production of polyunsaturated fatty acids would be obvious to one of ordinary skill in the art in light of the teachings available in the '952 specification.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

In the instant case, the claims are directed to an isolated nucleic acid comprising or complementary to at least 50% of the nucleotide sequence set forth as SEQ ID NO: 13. In claims 4 and 5 the nucleic acid is further limited to encoding a functionally active desaturase or being derived from *S. diclina*. Thus, the claims broadly encompass a genus of any nucleic acid molecule having 50% identity to the disclosed SEQ ID NO: 13, wherein the sequence might or might not encode a functional desaturase or be derived from *S. diclina*.

The Guidelines for Written Description state: "when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus" (Federal Register, Vol. 66, No. 4, Column 3, page 1106). "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or

by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus" (MPEP §2163(3)(a)(ii)).

In the instant case, the specification provides a single example of a nucleic acid which meets the limitations of the claimed genus (*i.e.,* the nucleic acid encoding the *S. diclina* Δ-6 desaturase). Beyond this single species, the specification is silent with regard to the relevant, identifying characteristics of the genus (i.e., those structural characteristics which confer useful function). Although the nucleic acid of claims 2, 3 and 5 is not limited to any particular function, a recitation of structural limitations alone, without a disclosed nexus between structure and function does not adequately describe the genus of nucleic acids encompassed by the claim because it is the function that is relied upon for patentable utility. Although claim 4 is limited to encoding a functionally active desaturase, the specification fails to set forth the structural requirements of a nucleic acid encoding a functionally active desaturase such that the skilled artisan could readily distinguish those nucleic acids which meet both the structural and functional limitations of the claims from those nucleic acids having only the structural characteristics. As the skilled artisan cannot distinguish those nucleic acids encompassed by the claims from those not encompassed by the claim, the specification clearly fails to provide the relevant, identifying characteristics of the claimed genus.

Furthermore, an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself. It is not sufficient to define DNA solely by its

principal biological property (i.e., it encodes a functional desaturase), because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any DNA with that biological property. Also, naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, claiming all DNA's that achieve a result without defining what means will do is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)).

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the broad class of nucleic acid comprising at least about 50% of the nucleotide sequence set forth as SEQ ID NO: 13. Therefore, only the described nucleic acid comprising SEQ ID NO: 13 and those encoding SEQ ID NO: 14 (the polypeptide encoded by SEQ ID NO: 13) meet the written description provision of 35 U.S.C. §112, first paragraph.

Claims 2-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid comprising SEQ ID NO: 13 or a nucleic acid encoding SEQ ID NO: 14, wherein said nucleic acid encodes a functionally active Δ-6 desaturase, does not reasonably provide enablement for any nucleic acid comprising or complementary to at least about 50% of the nucleotide sequence set forth as SEQ ID NO: 13. The specification does not enable any person skilled in the art to which it pertains, or with which

it is most nearly connected, to make or use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

Nature of the invention and Breadth of the claims: The elected invention is drawn to nucleic acids encoding a fungal Δ6-desaturase enzyme useful for the production of polyunsaturated fatty acids using recombinant DNA techniques. The claims broadly encompass any nucleic acid comprising or complementary to at least about 50% of the nucleotide sequence set forth as SEQ ID NO: 13, wherein the nucleic acid may or may not encode a functional desaturase enzyme.

State of the prior art and level of predictability in the art: Although the art provides several examples of nucleic acids encoding functional desaturase enzymes (see, e.g., US Pub. No. 2002/0156254), the art does not generally teach how one might use any nucleic acid having at least about 50% of the nucleotide sequence set forth as SEQ ID NO: 13 regardless of function. Furthermore, the art teaches that the effects of amino acid substitutions on the functional characteristics of a polypeptide are unpredictable. For example, Richards (1997) *Cell Mol. Life*

Sci. 53:790-802 teaches, "[i]n terms of structural alterations and thermostability, responses to genetic mutations are context dependent and remain difficult to predict with any confidence" (abstract, column 1). Thus, Richards teaches that the effect of mutation on protein stability, a prerequisite for biological function, is unpredictable. Richards also teaches that even limited amino acid modifications can have dramatic effects on protein structure and function. In the second column on page 791, Richards cites the example of influenza virus hemagglutinin protein, wherein alterations in the ionization state of just a few ionizable groups dramatically alters the biological behavior of the molecule. Citing a published study of done on the gene V protein, Richards teaches that, in spite of only limited modification at two amino acid positions, "[t]he effects on the overall stability of the protein were remarkably variable" (page 794, column 1). In the paragraph bridging pages 796 and 797, Richards teaches, "[i]n single site mutants, the structural changes are generally greatest near the site of mutation, and moving away, decrease radially in all directions. *Even the small changes are so complex that the linkage relations do not allow assignments of the energetic changes to unique parts of the altered residue and its immediate contacts*" (emphasis added) and "[t]here is no convincing explanation yet of how the changes in binding can produce a major movement over such a distance." Finally, in the first full paragraph in the second column on page 793, Richards teaches, "[a]lmost all mutations are accompanied by some conformational change, making prediction of the effects on stability difficult. *In most cases mutations lead to lowering of the stability.*" (emphasis added). Thus, Richards teaches that small changes in the primary structure of a protein frequently have dramatic effects on the higher order structure and function of the protein, and that these effects are highly unpredictable. Given these teachings, the skilled artisan would understand that most of

the polynucleotides having the structural limitations set forth in the claims would not encode a functional Δ6-desaturase.

Amount of direction provided by the inventor and existence of working examples: The disclosure provides a single example of a nucleic acid having the structural features of the claims (i.e., SEQ ID NO: 13) and demonstrates that the nucleic acid encodes a functional Δ6-desaturase that can be used according to the teachings of the specification to produce a polyunsaturated fatty acid in a recombinant host cell (see especially Example 4 and Table 1). However, the specification provides no guidance that would enable the skilled artisan to use any nucleic acid having at least about 50% of the nucleotide sequence set forth as SEQ ID NO: 13 and does not teach the skilled artisan how to make nucleic acids that can be used according to the teachings set forth in the specification without engaging in undue trial and error experimentation.

Relative skill of those in the art and quantity of experimentation needed to make or use the invention: Although the relative level of skill in the art is high, the skilled artisan would not be able to make and use the full scope of the claimed invention. The art teaches that the proteins are exquisitely sensitive to changes in amino acid sequence and the consequences of modifying amino acid sequence on the function of a protein are highly unpredictable. Therefore, in order to make any nucleic acid having at least about 50% of the nucleotide sequence set forth as SEQ ID NO: 13 and encoding a Δ6-desaturase that could be used according to the teachings of the specification, the skilled artisan would have to construct and test each nucleic acid having the structural features of the claimed nucleic acid for useful functional. Although the presence of inoperative embodiments within the scope of the claim does not necessarily render a claim non-enabled (see *Atlas Powder Co. v. E.I. du Pont de Nemours & Co* (224 USPQ 409, 414;

hereinafter *Atlas*). *Atlas* also provides, "[o]f course, if the number of inoperative combinations becomes significant, and in effect forces one of ordinary skill in the art to experiment unduly in order to practice the claimed invention, the claims might indeed be invalid" (page 414). In the instant case, the number of inoperative embodiments would clearly require that the skilled artisan engage in undue experimentation to practice the full scope of the claimed invention.

Thus, due to the art recognized unpredictability of the functional characteristics of nucleic acids having at least about 50% of the nucleic acid sequence set forth as SEQ ID NO: 13 and the lack of guidance in the specification or prior art with regard to how to make and use the full scope of the claimed subject matter it would require undue experimentation to practice the invention commensurate with the full scope of the claims.

Claims 11 and 13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing a desaturase in a host cell *in vitro* and an isolated host cell comprising a vector comprising the nucleic acid set forth as SEQ ID NO: 13, does not reasonably provide enablement for the method or host cell *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Nature of the invention and Breadth of the claims: Claim 11 are directed to a method of producing a desaturase comprising introducing a vector comprising the nucleic acid set forth as SEQ ID NO: 13 into a host cell, and claim 13 is directed to a host cell comprising a vector comprising the nucleic acid set forth as SEQ ID NO: 13. Given that the specification does not limit the host cells of the claims to *in vitro* and clearly contemplates production of desaturases in

transgenic animals (see, e.g., the paragraph bridging pages 28-29) the claims encompass a method of producing a Δ6-desaturase in a transgenic animal and a host cell in a transgenic animal. As the specification teaches that the claimed method and host cell are to be used to produced polyunsaturated fatty acids, the fully enabling disclosure must teach the skilled artisan how to make a transgenic animal useful for the production of a polyunsaturated fatty acid.

State of the prior art and level of predictability in the art: At the time of the effective filing date of the instant application the recombinant production of proteins in mammals for pharmacological use was in an early stage of development. In reviewing the relevant literature, Houdebine (*Transgen. Res.* (2000) 9:305-320) describes a myriad of obstacles that have been encountered by artisans seeking to express recombinant proteins in mammals at pharmaceutically relevant levels. In the abstract, Houdebine identifies three major sources of unpredictability in the art. First is the unpredictability of transgene expression; second is the unpredictability of proper posttranslational modification; and third is the unpredictable effects of high-level recombinant expression on the host mammal. Significantly, Houdebine teaches, "the mammary gland is presently the only really available animal bioreactor" (page 315, column 1, paragraph 7). Thus, at the time of filing, methods for pharmaceutically relevant production or recombinant proteins in mammalian organs and tissues outside of mammary gland were unavailable to the skilled artisan. With regard to production of pharmaceutical proteins in milk, Houdebine teaches, "numerous experiments have shown that the level and specificity of expression of a gene construct used as a transgene cannot be easily predicted" (paragraph bridging pages 309-310). In the paragraph bridging the left and right columns on page 311,

Houdebine teaches that even the best mammary-specific promoters available as of 2000 provided inconsistent and unpredictable results when used for expression of recombinant proteins *in vivo*.

Although the art teaches expression of a fungal Δ6-desaturase in cultured mammalian cells (see Kelder *et al.* (2001) *Mol. Cell. Biochem.* 219:7-11), Houdebine also points out that experiments carried out *in vitro* using cultured cells are poor predictors of expression *in vivo*. In the third paragraph in the first column on page 314, Houdebine states, "[cultured mammary] cells can at best predict the intrinsic potency of a construct for transcription but not the level of expression in transgenic animals. The cell lines are not expected to be able to reflect all the events, which mature the proteins post-transcriptionally." Houdebine further teaches that proper posttranslational processing of proteins expressed at pharmaceutically relevant levels is often unpredictable because the mechanisms are dependent on cellular enzymes that are present at variable concentrations in different cell types (paragraph bridging columns 1 and 2 on page 313). Importantly, because proper glycosylation is vital for pharmacological activity of many enzymes, Houdebine teaches that mammary cells do not always glycosylate recombinant proteins in an appropriate manner even when the protein is naturally secreted in milk in a glycosylated form (see the example of bile salt-stimulated lipase presented in the second full paragraph in the right column on page 313). Houdebine teaches that the reasons why some proteins are not correctly glycosylated are particularly complex and might be related to the superphysiolgical production of the recombinant protein.

When viewed as a whole, the teachings of Houdebine, which are based on a review of the art as of 2000, clearly show that obtaining pharmaceutically useful expression of a protein in a mammal was only enabled for a limited set of proteins in mammary tissues, and production of

pharmaceutically useful amounts of any given protein in mammary tissue was unpredictable. As the art does not provide teachings that would enable the skilled artisan to make a mammal capable of producing a pharmaceutically useful amount of a Δ6-desaturase, the skilled artisan must rely on the specification for guidance as to how to make the claimed invention without undue experimentation.

Amount of direction provided by the inventor and existence of working examples: The instant specification discloses a nucleic acid encoding a *S. diclina* Δ6-desaturase and demonstrates heterologous expression of the Δ6-desaturase in *S. cerevisiae* (*Id.*). In the paragraph bridging pages 28-29, the specification provides prophetic teachings that a transgenic mammal may be used to express to express the Δ6-desaturase to provide altered levels of polyunsaturated fatty acids in milk, tissue or other fluid samples. However, the specification provides no specific guidance with regard to making a transgenic animal capable of expressing a *S. diclina* Δ6-desaturase such that useful altered levels of polyunsaturated fatty acids can be obtained.

Relative skill of those in the art and quantity of experimentation needed to make or use the invention: Although the relative level of skill in the art is high, the ordinary skilled artisan would not be able to make the full scope of the claimed invention without engaging in undue experimentation. The specification teaches that the *S. diclina* Δ6-desaturase can be expressed in a transgenic animal and that that animal can be used to provide polyunsaturated fatty acids for use in pharmaceuticals and for nutrition. However, the art teaches that obtaining expression of heterologous proteins *in vivo* to produce genetically modified animals capable of functioning as bioreactors is highly unpredictable. Although, the specification demonstrates functional

expression of the Δ6-desaturase in yeast and the art teaches that functional fungal Δ6-desaturases can be expressed in mammalian cells, the art teaches that results obtained in cultured cells cannot readily be extended to *in vivo* expression systems. The specification provides no evidence that a useful transgenic bioreactor can be obtained by expressing the fungal Δ6-desaurase *in vivo* without significant empirical experimentation to overcome the art-recognized barriers to obtaining useful *in vivo* expression. Thus, practicing the method of claim 11 *in vivo* or making the cell of claim 13 *in vivo* such that it could be used for the purposes asserted in the specification would require undue experimentation. For these reasons, the disclosure fails to provide enablement for the full scope of the claimed subject matter.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim is directed to a nucleic acid "derived from" *S. diclina*. Without a clear statement of the process by which the starting material is derivatized it is not possible to know the metes and bounds of such a limitation because any given starting material can have many divergent derivatives depending on the process of derivatization.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 703-305-4448. The examiner can normally be reached on Monday through Friday 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 703-305-1998. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

DMS

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER